REMARKS

The September 3, 2008 Official Action has been carefully considered. In view of the amendment submitted herewith and these remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set in the September 3, 2008 Official Action. The initial due date for response, therefore, was December 3, 2008. A petition for a two (2) month extension of the response period is included with this amendment and request for reconsideration, which is being filed before the expiration of the two (2) month extension period.

It is also noted preliminarily that as a result of the restriction requirement set forth in the preceding Official Action, non-elected method claims 10-35 have been withdrawn from consideration in this application. In accordance with the decisions in *In re Ochiai,* 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996) and the Notice published in the Official Gazette on March 26, 1996, setting forth guidelines for the treatment of restricted product and process claims (see 1184 OG 86), applicants respectfully request that, in the event the claims of elected Group I (claims 1-9) are found allowable, then the method claims of Group II (claims 10-35) be rejoined and examined for patentability. See §821.04 of the Manual of Patent Examining Procedure.

Turning to the substantive aspects of the September 3, 2008 Official Action, claims 1 and 4 stand rejected under 35 USC §102(b) as allegedly anticipated by Hcaplus 60:69598, which discloses the compound 5-hydroxy-6-methyl-4-(N-4H-1,2,4-triazol-4-ylformimidoyl)-3-pyridinemethanol, 3-(dihydrogen phosphate).

Claim 7 has been rejected under 35 USC§102(b) as allegedly anticipated by U.S. Patent 5,962,687 to Maidonis and Schneider (hereinafter "Maidonis"), which is cited for its disclosure of para-phenetidyl-pyridoxal.

Claims 2, 3 and 5 have been rejected under 35 USC §103(a) as allegedly unpatentable over the above-cited Hcaplus 60:69598. According to the examiner, it would have been obvious to one of ordinary skill in the art to make pharmaceutical compositions out of the compounds disclosed in the cited reference because it is purportedly obvious to place these compounds in ethanol or another non-toxic solvent in which they are soluble, due to their solubility in such

solvents.

Claim 7 has been further rejected under 35 USC §103(a) as allegedly unpatentable over Maidonis. In support of this rejection, the examiner contends that it would have been obvious to one of ordinary skill in the art to make pharmaceutical compositions out of para-phenetidyl-pyridoxal because it is obvious to place this compound in ethanol or another non-toxic solvent in which they are soluble, due to their solubility in such solvents.

Claims 2-9 have been rejected for allegedly failing to satisfy the enablement requirement of 35 USC §112, first paragraph. While acknowledging that the specification is enabling for treating some flaviviral infections and diseases associated with such infections, the examiner contends that the specification does not reasonably provide enablement for treating all viral infections or associated diseases or prevention of any viral infection or associated disease.

The foregoing rejections constitute all of the grounds set forth in the September 3, 2008 Official Action for refusing the present application.

In accordance with the present amendment, claims 1 and 4 have been amended by excluding "triazole" as a possible heterocyclic radical represented by "R" in the formulas set forth therein.

Claim 7 has been amended by excluding ethoxyphenyl as a possible substituted arakyl radical represented by R in the formula set forth therein.

The present amendment to claims 1, 4 and 7 cannot be regarded as involving new matter, when considered in light of *In re Johnson,* 194 USPQ 187 (CCPA 1977) or *In re Driscoll*, 195 USPQ 434 (CCPA 1977), which stand for the proposition that an applicant for patent may narrow his or her claims, for example, by exclusion of specific compounds or substituents, to avoid having them read on subject matter which applicant is not entitled to claim.

Claims 2, 5 and 8 have been amended to conform substantially to the preamble of original claim 10. As a result of this amendment, claims 2, 5 and 8 no longer refer to preventing viral infection.

The preamble of claims 4 and 7 have been amended by deleting the statement of intended use, which is not required for patentability. Compare claim 1.

Claim 10 has also been amended to delete the words "or preventing" so that method claims 10-35 will avoid the present ground of rejection under 35 USC §112, first paragraph, in

the event that claims 10-35 are rejoined for examination in this application, as requested above.

No new matter has been introduced into this application by reason of the present amendment, entry of which is hereby respectfully requested.

For the reasons set forth below, applicants respectfully submit that all of the grounds of rejection set forth in the September 3, 2008 Official Action cannot be maintained in view of the present amendment. These grounds of rejection are, therefore, respectfully traversed.

A. The 35 USC §102(b) Rejection of Claims 1 and 4 as Allegedly Anticipated by Hcaplus 60:69598 Cannot be Maintained in View of the Present Claim Amendment

Rejections under 35 USC §102(b) are proper only when the claimed subject matter is identically disclosed or described in the prior art cited as evidence of anticipation. *In re Arkley,* 172 USPQ 524 (CCPA 1972). Applying this rule of law to the present case, the 35 USC §102(b) rejection of claims 1 and 4 based on Hcaplus 60: 69598 is clearly improper because the cited reference fails to identically disclose or describe the subject matter of the rejected claims as now amended. Accordingly, the §102(b) rejection of claims 1 and 4 based on Hcaplus 60:69598 is untenable and should be withdrawn upon reconsideration.

Nor can Hcaplus 60:69598 reasonably be regarded as rendering claims 1 and 4 *prima facie* obvious.

Hcaplus 60:69598 appears to be devoid of any disclosure of suggestion regarding any practical utility for the compounds disclosed therein. It has long been held that where, as here, a prior art reference neither discloses nor suggests a utility for the compound described therein, it cannot be maintained that the reference renders obvious a related structure, when a person having ordinary skill in the art (per §103(a)) would know of no practical reason to make the reference compound, much less any structurally related compound. *In re Stimniski,* 170 USPQ 343, 347 (CCPA 1971).

In summary, it must be concluded that the compounds now claimed in claims 1 and 4 are patentably distinguishable over the compound disclosed in Hcaplus 60: 69598.

B. The 35 USC §102(b) Rejection of Claim 7 as Allegedly Anticipated by Maidonis Cannot be Maintained in View of the Present Amendment

Maidonis fails to provide evidence of anticipation with respect to claim 7 as now amended for essentially the same reason set forth above in discussing the untenability of the §102(b) rejection of claims 1 and 4 based on Hcaplus 60:69598. There is no disclosure or description in Maidonis of the compounds of claim 7, as now amended. Consequently, this ground of rejection is untenable and should be withdrawn upon reconsideration.

Maidonis likewise fails to render obvious the compounds now claimed in claim 7. According to the disclosure of Maidonis, para-phenetidyl-pyridoxal is an intermediate in the method for producing magnesium pyridoxal-5′-phosphateglutamate described therein. However, the mere fact that Maidonis' para-phenetidyl-pyridoxal is used as an intermediate in the production of the corresponding magnesium pyridoxal-5′-phosphateglutamate does not provide adequate motivation for a person having ordinary skill in the art to stop the Maidonis synthesis and investigate the intermediate para-phenetidyl-pyridoxal with an expectation at arriving at applicants' claimed pyridine derivatives having utility as anti-viral agents. This is so, notwithstanding the indication in Maidonis regarding the benefit of drying p-phenetidyl-pyridoxal in order to achieve an optimal reaction course. *Cf., In re Lalu*, 223 USPQ 1257, 1260 (CCPA 1984).

C. The 35 USC §103(a) Rejection of Claims 2, 3 and 5 Cannot be Maintained in View of the Present Amendment

A rejection under 35 USC §103 is proper only when the invention as a whole is shown to be obvious in view of the prior art. Thus, all claim recitations must be considered in determining obviousness over the prior art. *In re Boe*, 184 USPQ 38 (CCPA 1974). Moreover, since chemical compounds and compositions are inseparable from their properties, the properties of a claimed compound or composition must also be considered as part of the "invention as a whole" in assessing patentability under 35 USC §103. *In re Albrecht*, 185 USPQ 585 (CCPA 1975).

As a result of the present amendment, Hcaplus 60:69598 fails to satisfy all of the recitals of claims 2, 3 and 5, in that Hcaplus 60:69598 neither teaches nor suggests the compounds called

for in the claimed composition, as previously discussed. Accordingly, this ground of rejection is untenable and should be withdrawn upon reconsideration.

D. The 35 USC §103(a) Rejection of Claim 7 Cannot be Maintained in view of the present Amendment

The 35 USC §103(a) rejection of claim 7 as allegedly obvious over Maidonis is untenable based on essentially the same rationale discussed above in relation to the untenability of the §103(a) rejection of claims 2, 3 and 5 over Hcaplus 60:69598. Accordingly, this ground of rejection should be withdrawn upon reconsideration.

E. The 35 USC §112, First Paragraph, Rejection of Claims 2-9 for Alleged Insufficient Enablement Cannot be Maintained in View of The Present Amendment

The law is well-settled that whenever a rejection based on inadequacy of enablement is made, it is incumbent upon the Patent and Trademark Office to explain why the truth or accuracy of the applicants' disclosure is doubted, and to back up any such doubt with acceptable evidence of reasoning which is inconsistent with the contested disclosure. *In re Marzocchi,* 169 USPQ 367 (CCPA 1971). A properly supported showing that applicants' disclosure entails undue experimentation is part of the PTO's burden under §112, first paragraph. *In re Angstadt*, 190 USPQ 214 (CCPA 1976).

In the present case, applicants' specification clearly satisfies the "how to make" and "how to use" requirements of 35 USC §112 with respect to the currently amended claims. Included in the present specification are numerous examples which describe the preparation of diverse compounds falling within the scope of the structural formulas of claims 1, 4 and 7. Biological activity, based on results of standard RdRp assay testing of representative compounds, is set forth at pages 32-34 of the specification. The test results show that the compounds of the invention are effective at inhibiting RNA synthesis by RdRp enzymes involved in flavivirus replication. In this respect, the present case is readily distinguishable from *Ex parte Sudilovsky*, 21 USPQ2d 1702 (PTO BPAI), which is cited at page 8 of the September 3 Official Action.

The specification also gives detailed guidance concerning the preparation of

pharmaceutical compositions comprising the pyridine derivatives of the invention, the appropriate amount of the active agent to be administered, as well as suitable routes of administration.

By suggesting that applicants must provide evidence of efficacy in humans based on clinical trials, the examiner is in effect demanding proof of commercial usefulness, which is not the statutory standard of utility under the U.S. patent statutes. As stated in *In re Anthony,* 162 USPQ 594, 605 (CCPA 1969), commercial usefulness has never been a prerequisite for a reduction to practice and the subsequent patentability of any of the classes of patentable subject matter set forth in §101, much less the particular class of compositions of matter called drugs.

It is noteworthy in this regard that the PTO has issued quite a number of patents claiming compounds and methods for the treatment of flaviviridae infection. See, for example, U.S. Patents Nos. 6,841,561, 6,887,877, 7,101,861, 7,105,493, 7,148,206 and 7,163,929. None of these patents appear to provide data evidencing clinical treatment of viral infections and associated disease. According to the examiner, it is the lack of such data that renders applicants' specification deficient under 35 USC §112, first paragraph. The PTO's issuance of the aforementioned patents shows beyond doubt, however, that such data is not a prerequisite to patentability.

Furthermore, it was held in *Cross v. Iizuka,* 224 USPQ 739 (Fed. Cir. 1985) that evidence of *in vitro* utility only is sufficient to satisfy the statutory utility requirement. In the present case, as in *Cross v. Iizuka, supra,* applicants have presented clear evidence showing anti-flavivirus activity *in vitro* for the inhibition of RNA synthesis by RdRp enzyme involved in flavivirus replication. As the court observed in *Cross v. Iizuka, supra,* "[s]uccessful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public. . ." *Id.* at 748.

Not only is the examiner's position concerning insufficient enablement contrary to the relevant case law, it contravenes the fundamental purpose of the U.S. patent system, which is to promote progress in the useful arts. Pharmaceutical research is fueled, in part, by the promise of patent protection on compounds that are discovered to have the desired pharmacological activity. To require a showing of clinical efficacy in humans prior to submission of a patent application creates a genuine disincentive to carrying out pharmaceutical research. *In re Fisher,* 166 USPQ

18 (CCPA 1970), which is cited by the examiner in support of the insufficient enablement rejection of claims 2-9, is readily distinguishable from the present case on its facts. In *Fisher*, the Court disallowed a claim to an ACTH preparation, including an open-ended recitation of ACTH potency, i.e., at least one international unit of ACTH per milligram. In view of the limited disclosure of ACTH potencies provided in the specification, which were only in the range of 1.11 to 2.30 IUs of ACTH per milligram. In the present case, by contrast, the scope of applicants' claims is not open-ended, but is sharply defined and unquestionably warranted in view of the number of representative examples provided in the present specification.

Moreover, unlike the applicant in *In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993), applicants in this instance are not attempting to extrapolate to all members of a very diverse and genetically complex group of RNA viruses, the success obtained with a single viral species.

On the present record, it is clear that the examiner has failed to present evidence or reasoning which would tend to substantiate the doubts expressed concerning the sufficiency of applicants' disclosure insofar as presently amended claims 2-9 are concerned. In the absence of such evidence or reasoning, the 35 USC §112, first paragraph, rejection of claims 2-9 is untenable and should be withdrawn upon reconsideration.

In view of the amendment submitted herewith and the foregoing remarks, it is respectfully urged that the rejections set forth in the September 3, 2008 Official Action be withdrawn and that this application be passed to issue, and such action is earnestly solicited.

Respectfully submitted,

DANN DORFMAN HERRELL and SKILLMAN, P.C.
Attorneys for Applicant

By Patrick J. Hagan

Patrick J. Hagan
Registration No. 27,643

Customer Number 00110